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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,916	10/10/2001	Peter M. Thule	US 1292/01 (VA)	4645

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,916	THULE, PETER M.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date [illegible]
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 4/21/04. Claims 1-21 are pending in the application and are addressed herein.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-16) and the species that is SEQ ID NO. 5, in the reply filed on 4/21/04 is acknowledged. The traversal is on the ground(s) that the MPEP indicates that up to 10 sequences can be examined without restriction. This is not found persuasive because although the MPEP states that up to 10 sequences ***may*** be examined without restriction, PTO management has indicated that *may* does not mean *must* and that restriction to a single sequence is apropriate. In the instant case, it is respectfully pointed out that the sequences are not subject to group restriction, but that the sequences are species and should the elected species be found novel, the examiner will continue to examine the other species until a non-novel sequence is found.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Additionally, claims 17-21 and the non-elected species are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/21/04. It is acknowledged that should claims 1-16 become allowable, withdrawn claims will be subject to rejoined as indicated and according to the rules indicated in the previous communication.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim is drawn to **a transgene** comprising the construct of claim 1. However, the specification does not appear to describe a transgene in any other context than a transgene that is part of a vector construct. It is acknowledged that one of ordinary skill in the art would recognize the term "transgene" as a gene that is not a naturally endogenous gene, however, this definition requires that the transgene be in a cell or a animal (such as a transgene in a transgenic animal). With respect to the term transgene being a gene in a cell or animal it is unclear how a transgene can comprise the construct of claim 1, as "gene" typically refers to only the coding sequence of a nucleic acid, such as a cDNA or genomic DNA. The specification only appears to describe a construct comprising a transgene that is operably linked to the GIRE and ISS promoter elements. However, the claim is not drawn to a construct comprising a transgene, but rather to a transgene comprising the construct of claim 1. Here, again, it is unclear how a transgene (typically only the coding sequence cDNA or gDNA) can comprise the construct of claim 1. It is noted that amending the claim to the construct of claim wherein said construct comprises a transgene would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

The instant claims are drawn to an insulin regulator construct comprising **a GIRE of a L-PK gene promoter**, **an insulin-sensitive element of an IGFBP-1** (claim 1), **a HNF-4 binding site and a glucose responsive site** (claim 2), as well as **a derivative** of the construct of claim 1 (claim 16).

These elements constitute different genuses of sequences that are different from the sequences explicitly described in the specification. As such, the claims encompass an enormous

number of species that belong to each claimed genus of molecules. To be clear, the claims encompass a genus of GIREs, a genus of insulin-sensitive elements, a genus of HNF-4 binding sites, a genus of glucose responsive elements and a genus of constructs wherein each genus encompasses a huge number of different species, considering the genuses encompass any sequence which would retain the desired function but which is different from any sequences described. Furthermore, applicant has not disclosed the structural feature which are responsible for the function of the genus molecules. That is, applicant has not indicated any structure-function relationship for the genus of molecules encompassed by the claims such that disclosure clearly indicates which molecules have the required function. Without such a disclosure, the applicant has not adequately described a sufficient number of genus of molecules. It is noted that applicants have only disclosed a single GIRE, a single insulin-sensitive element, a single HNF-4 binding site and NO derivatives of the construct of claim 1 has been described.

Additionally, claims 1-9 and 10-16 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement in view of the written description rejection set forth above. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As mentioned above, the claims encompass sequences for which there is insufficient written description provided in the specification and includes sequence comprising substitutions, fragments, variants and derivatives of the disclosed sequences. Without a clear indication of the sequences encompassed by the claims one of skill in the art would not know how to make or use

the claimed invention without performing an undue amount of additional experimentation in order to first identify the sequences that had the desired functions.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. It is noted that the claims are drawn to an insulin regulator construct; however, it is essential that all insulin regulator construct comprises a nucleic acid encoding insulin or proinsulin, otherwise the construct would not be a n insulin regulator construct as it would not regulate insulin levels in a subject or model system. Therefore it is critical/essential that the claims additionally comprise the limitation that the construct includes a nucleic acid sequence encoding insulin or proinsulin operably linked to the construct in order to be able to practice the invention. Without such a limitation in the claim(s) the claims are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). It is noted that amending the independent claims to include the limitation that the construct comprises a sequence encoding insulin or proinsulin operably linked to the promoter elements of the construct would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Thule et al. (Gene Therapy, 2000, Vol 7, pages 205-214- cited on IDS).

It is noted that, in the interest of compact prosecution, claim 14 will be interpreted as the construct of claim 1 further comprising a transgene operably linked to the construct.

The instant claims are drawn to an insulin regulator construct comprising a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter wherein glucose increases the expression of a sequence operably linked to the construct and wherein insulin suppresses the expression of a sequence operably linked to the construct. It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which comprises an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

Thule teaches an adenoviral vector comprising all of the claimed elements, and also named the vector Ad/$(GIRE)_3$BP-1 2xfur (e.g., see abstract, Fig. 1). Also note that all of the figures describing the Ad/$(GIRE)_3$BP-1 2xfur vector in Thule appear to be identical to Figures found in the instant application. As such, Thule clearly anticipates the insulin regulator construct claimed in claims 1-16.

Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Diabetes May 1999, supplement—cited in IDS).

It is noted that, in the interest of compact prosecution, claim 14 will be interpreted as the construct of claim 1 further comprising a transgene operably linked to the construct.

The instant claims are drawn to an insulin regulator construct comprising a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter wherein glucose increases the expression of a sequence operably linked to the construct and wherein insulin suppresses the expression of a sequence operably linked to the construct. It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which comprises an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

Thule teaches an adenoviral vector comprising all of the claimed elements, and also named the vector Ad/$(GIRE)_3$BP-1 2xfur (e.g., see abstract). As such, Thule clearly anticipates the insulin regulator construct claimed in claims 1-16.

Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Abstract from meeting June 9-13, 1999—cited in IDS).

It is noted that, in the interest of compact prosecution, claim 14 will be interpreted as the construct of claim 1 further comprising a transgene operably linked to the construct.

The instant claims are drawn to an insulin regulator construct comprising a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter wherein

glucose increases the expression of a sequence operably linked to the construct and wherein insulin suppresses the expression of a sequence operably linked to the construct. It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which comprises an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

Thule teaches an adenoviral vector comprising all of the claimed elements, and also named the vector Ad/$(GIRE)_3$BP-1 2xfur (e.g., see abstract). As such, Thule clearly anticipates the insulin regulator construct claimed in claims 1-16.

Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Abstract from meeting June , 1998—cited in IDS).

It is noted that, in the interest of compact prosecution, claim 14 will be interpreted as the construct of claim 1 further comprising a transgene operably linked to the construct.

The instant claims are drawn to an insulin regulator construct comprising a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter wherein glucose increases the expression of a sequence operably linked to the construct and wherein insulin suppresses the expression of a sequence operably linked to the construct. It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which comprises an adenoviral vector comprising 3

GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

Thule teaches an adenoviral vector comprising all of the claimed elements, and also named the vector Ad/$(GIRE)_3$BP-1 2xfur (e.g., see abstract). As such, Thule clearly anticipates the insulin regulator construct claimed in claims 1-16.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-8656. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0756. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER